REMARKS

Upon entry of this paper no claims have been amended, no claims have been canceled and no new claims have been added. Now pending in the application are claims 46-48, 50-52, 55-57, 69-74, 76-82, 84-89 and 92-101, of which claims 46, 50, 52, 57, 69, 77, 78, 81, 88, 92, 93, 96, 97, 99 and 100 are independent. For the reasons that follow, Applicants respectfully submit that the claims define over the art of record and should be passed into allowance.

Claim rejections under 35 U.S.C. §102

Claims 46-48, 50, 51, 69-74, 76-82, 84-89 and 92-101 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al. (hereafter Miller). Applicants respectfully traverse the rejection with the following remarks.

The Miller reference is generally directed to forming an anatomical textbook (template) from measurements conducted on a single patient, and applying the anatomical textbook to studies of a particular patient by using transformations to deform the spatial configuration of the studies of the particular patient until they register with the anatomical textbook (page 11945, column 2, paragraph 2). Once the most realistic (most probable) transformations have been determined, studies of the particular patient may be mapped onto the anatomical textbook allowing identification of brain structures. The Miller reference uses a "Bayesian view" (Bayesian inference analysis) to determine the most realistic or most probable spatial transformation that would spatially transform the data from patient A to match the anatomical template, (page 11945, column 2, paragraph 4). In Bayesian analysis, first, a prior distribution is assumed (page 11945, column 2, paragraph 4). In Miller, the assumed prior distribution is the assumed spatial configuration of the brain for particular patient A, (page 11945, column 2, paragraph 4). In the Bayesian view, applying a transformation to the assumed prior distribution (the spatial configuration of the brain of patient A) results in the Bayesian posterior distribution (the anatomical template spatial configuration). The most realistic and most probable transformation is determined by finding the particular parameters that minimize the sum of a "displacement" potential energy term and the elasticity potential energy term (page 11945, column 2, paragraph 4). After the studies of the brain of patient A are mapped onto the anatomical template using the most probable transformation, the brain structures of patient A can

be identified. The Miller reference also describes applying the anatomical template, formed from MR data from a single subject, to a different particular patient, patient B (page 11947, column 1, paragraphs 3-5).

In contrast, an embodiment of the pending application is generally directed to a prior probability MR based atlas that contains values representative of magnetic properties of a magnetic resonance (MR) scan and prior probability data relating to tissue type for at least one subject. The tissue type prior probability is derived from measurements of at least one subject, and preferentially the tissue type prior probability may be derived from measurements of a plurality of subjects. A tissue type prior probability is the probability that a particular voxel contains a particular tissue type based on the tissue type found in the particular voxel for each subject used to form the atlas, as described in the specification from page 11, line 21 to page 12, line 16 and in Figures 9A and 9B. If an atlas is formed using information from more than one subject, a given node corresponding to a given voxel in the atlas may have more than one tissue type prior probability, each associated with a different tissue type, because different tissues types may have been found at the particular voxel for different subjects. As illustrated in Figures 5 through 8, the magnetic properties of a particular voxel for subjects with a first tissue type may be calculated and stored separately than the magnetic properties of the particular voxel for subjects with a second tissue type. A tissue type can include general categories of tissue type such as gray matter, white matter and cerebral spinal fluid. The tissue type can also include an appropriate anatomical structure label such as the hippocampus.

"a prior probability MRI based atlas" including "tissue type prior probability," as recited by independent claims 46, 77, 78, 81, and 92.

The Miller reference fails to disclose a "*prior probability MRI based atlas*," including "*tissue type prior probability*," as recited in independent claims 46, 77, 78, 81 and 92. The Office Action states that the Miller reference "describes a procedure in which an elastic model of the brain anatomy is driven by data-overlap probabilities to warp brain atlas images onto MRI slice or section images," and cites the abstract. The probabilities to which the Office Action refers are the probabilistic transformations for deforming a spatial configuration of the brain of subject A until it registers with the spatial configuration of the anatomical template, (page 11945, column2, paragraphs 2-3). In contrast, a *tissue type prior probability* is the probability

that a particular voxel contains a particular tissue type based on the tissue type found in the particular voxel for each subject used to form the atlas, (page 11, line 21 to page 12, line 16 and in Figures 9A and 9B). As described in the specification and claimed in claim 46, the *tissue type prior probability* is *derived from* a subject whose data is used to form the atlas. A probabilistic transformation for spatially registering data from a particular subject with data in the anatomical template is not a *tissue type prior probability* derived from measurements of the subject or subjects used to form the atlas.

The Office Action does not state that Miller discloses *tissue type prior probability*, because Miller does not disclose *tissue type prior probability*. The Office Action describes "each of the nodes configured to store at least two magnetic property values such as T1 and T2 values for each of the voxels, where the magnetic property values correspond to tissue type at one of [sic] more voxels," and cites (page 11947 column 1, paragraphs 3-5). The Miller reference describes an anatomical textbook (template) that "consists of a 4-touple of three MR images and a hand labeled segmentation," with the segmentation identifying "various gray matter nuclear regions: thalamus, putamen, ...," (page 11947, column 1, paragraphs 3). Hand labeled segmentation is not tissue type prior probability. The anatomical textbook is not a *prior probability MRI based atlas* that contains *tissue type prior probability*. The Miller reference fails to disclose each and every element of independent claim 46, 77, 78, 81, and 92 and their dependent claims 47, 48, 79, 80, 82 and 84-87, which are therefore allowable. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 46-48, 77-82, 84-87 and 92.

"a prior probability MRI based atlas,"
as recited by independent claims 50, 69, 88, 93, 96, 97, 99 and 100

The Miller reference does not disclose "*a prior probability MRI based atlas,*" as recited by independent claims 50, 69, 88, 93, 96, 97, 99 and 100. As described above, a prior probability of a property for a voxel is the probability that the voxel has a particular property based on the whether the corresponding voxel has that property in the data for each of the subject or subjects that are used to form the atlas. In the specification, as an illustrative example, prior probability is explained with respect to tissue type for a particular voxel. A tissue type prior probability for a voxel is the probability that a particular voxel contains a particular tissue type based on the tissue type found in the corresponding particular voxel for each subject used to

form the atlas, as described in the specification from page 11, line 21 to page 12, line 16 and in Figures 9A and 9B. The specification also describes global prior probabilities which "indicate the overall prior probability of something, such as a tissue type appearing in a particular area, or anywhere, in a subject," (page 12, lines 17-22). The global prior probabilities are derived from whether something, such as tissue type appearing in a particular area, exists in the subjects that form the atlas. As discussed above, the Miller reference discusses probabilistic transformations, but the Miller reference does not discuss *prior probabilities*; thus, Miller does not disclose a *prior probability MRI based atlas*. The Miller reference does not disclose each and every element of independent claims 50, 69, 88, 93, 96, 97, 99 and 100, and their dependent claims 51, 70-74, 76, 89, 94, 95, 98 and 101, which are therefore allowable. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 50, 51, 69-74, 76, 88, 89 and 93-101.

"a prior probability MRI based atlas" including data from "a plurality of subjects" as recited by claims 48, 51, 69, 78, 81, 88 and 95

In addition to the arguments above, Applicants assert that the Miller reference further fails to disclose "*a prior probability MRI based atlas*" that includes data from a *plurality of subjects* as recited by claims 48, 51, 69, 78, 81, 88 and 95. Claims 48 and 95 recite "*data derived from a plurality of subjects...*" Claim 69 recites magnetic property values for each of said voxels "*as determined by magnetic resonance imaging of a plurality of subjects.*" Claims 78 and 81 recite "*corresponding to a tissue type for each of a plurality of corresponding voxels of a plurality of subjects,*" and claim 88 recites "*correspond to a plurality of subjects.*" Claim 95 recites "*data derived from a plurality of subjects.*"

Some embodiments of the present invention use MRI measurements from a *plurality of subjects* to build an accurate prior probability MRI based atlas that includes tissue type. Such an atlas, derived from MRI measurements of previous subjects, can be used to segment and/or align MR scans of new subjects. Figures 9A and 9B and page 11, line 19, to page 12, line 13, provide an illustrative example of how prior probabilities of tissue types for a single node are calculated from MR measurements of a plurality of subjects. From page 12, line 23, to page 14, line 23, and in Figures 10 and 11, the specification provides a detailed description for construction of a

prior probability MRI based atlas that include tissue type. The specification explains how incorporating data from a plurality of subjects increases the accuracy of the atlas.

The Office Action asserts that the Miller reference teaches generating an "MR based template or atlas from subjects with symbolic information that includes ... (page 11945, col. 1, paragraph 3)." The cited section of the Miller reference does not disclose generating a single MR based atlas from a plurality of subjects. In the cited section, the Miller reference describes an anatomical textbook (template) from a manually segmented study of a single subject, "an MR study of a normal patient at Duke University," (page 11947, column 1 paragraph 3). The Office Action also asserts that the Miller reference teaches determining statistical representation values...of the plurality of subjects (page 11945, col. 2, paragraph 5 – page 11946, col 1.)" In the aforementioned cited section, the Miller reference discloses how to apply the anatomical textbook (created with data from one patient) to a study of a different patient, "The information in the anatomical textbook (Ω, T,$\mathcal{T}$) is brought into the coordinates of the patient by finding the transformation $h \in \mathcal{H}$ on Ω which registers the studies [of the different patient] with the textbook," (page 11945, column 1, paragraph 2). Applying an anatomical template to a patient is not an atlas including data from a *plurality of subjects*. The Office Action also describes how the Miller reference applies the anatomical template (created using data from one subject) to patient A to identify brain structures, and how the Miller reference applies the same original anatomical template (created using data from one subject) to patient B to identify brain structures. Applying the same anatomical template to different patients is not forming a prior probability MRI based atlas including data from a *plurality of subjects*. The Miller reference does not disclose *a prior probability MRI based atlas* including data from *a plurality of subjects*. Thus, the Miller reference does not disclose each and every element of independent claims 48, 51, 69, 78, 81, 88 and 95, and their dependent claims 79, 80, 82, 84-87 and 89, which are therefore allowable. Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 48, 51, 69, 78- 82, 84-89 and 95.

Claim rejections under 35 U.S.C. §103

Claims 52 and 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (hereafter Miller) in view of U.S. Patent number 6740883 to Stodilka et al. (hereafter Stodilka) Applicants respectfully traverse the rejection with the following remarks.

The Stodilka reference is generally directed to a method of applying scatter and attenuation correction to emission tomography images of a region of interest of a patient under observation. The method "infers" the distribution of density within the region of interest using a computer model, without having to take transmission measurement of the region of interest, (column 1, line 65 to column 2, line 9). The Stodlika reference discusses a three dimensional computer model or "atlas" of the region of interest, which provides accurate density distribution...," (column 4, lines 54-59). The atlas includes two components, "a functional component simulating a "SPECT or PET scan of the region of interest and an anatomical component simulating a transmission scan of the region of interest," (column 4, lines 59-63). Data to construct a cardiac atlas "can be obtained in a variety of ways including "X-ray CT, MRI . . . Also, the cardiac atlas can be constructed by amalgamating a plurality of patient scans," (column 6, lines 61-67).

A combination of Miller and Stodilka is not the claimed invention

The Miller reference teaches a specific method of determining spatial transformations that map studies (data sets) of a particular patient on to an anatomical template (formed from scans of one person) to register the studies with the anatomical template. The Stodlika reference teaches a spatial transformation that maps atlas space onto patient-specific space for applying scatter and attenuation correction to emission tomography images, (column 7, lines 9-11). The spatial transformations discussed in the references map anatomical atlas space onto patient space and vice versa. The aforementioned transformations do not teach or suggest "*correcting distortion of*" a "*magnetic resonance modality volume*," as recited in claim 52. Emission tomography imaging, which involves injecting a radioactive isotope into a patient and detecting radiation emitted from the patient, is a completely different technology from magnetic resonance imaging, which involves detecting nuclear spin relaxation in a patient after RF excitation in a magnetic field gradient. Scatter and attenuation correction for emission tomography images as

taught by the Stodilka reference is totally unrelated to correcting distortion of a magnetic resonance modality volume.

A combination of the Miller reference and the Stodilka reference would provide many ways of spatially transforming between patient space and anatomical atlas space for both brains and hearts, and provide scatter and attenuation correction for emission tomography images. However, one of ordinary skill in the art could not combine the Miller reference and the Stodilka reference to generate *a method for creating a prior probability MRI based atlas* including *correcting distortion of said first magnetic resonance modality volume* (pertaining to a first subject) and *correcting distortion of said second magnetic resonance modality volume* (pertaining to a second subject) and *updating said magnetic property data in said node of said atlas*, as recited by independent claim 52. Hence, the result of combining the Miller reference and the Stodilka reference is not the Applicants' invention recited in independent claim 52.

Claims 52 and 55-57

The Stodilka reference and the Miller reference, alone or in combination, do not teach or suggest each and every element of independent claim 52. Specifically, the Stodilka reference and the Miller reference do not teach or suggest, a method for creating "*a prior probability MRI based atlas*" comprising "*providing a first magnetic resonance modality volume pertaining to a first subject...correcting distortion of said first magnetic resonance modality volume*" and "*recording a magnetic property value in a node of said atlas corresponding to a voxel of said first magnetic modality volume*" as recited by independent claim 52. The Stodilka reference and the Miller reference further fail to teach or suggest "*providing a second magnetic resonance modality volume pertaining to a second subject... correcting distortion of said second magnetic resonance modality volume; and updating said magnetic property data in node of said atlas....*," as recited by independent claim 52.

As conceded in the Office Action "Miller et al. do not explicitly teach the steps of correcting distortion during the registration process." The Office Action asserts that the Stodilka reference teaches "aligning subsequent scans to the atlas while correcting distortion which may include shifting, rotation, scaling, and/or non-linear operations," and cites col. 7, lines 7-10. The cited section of the Stodilka reference describes how the atlas may be applied to a scan of a

specific patient, but it does not describe how to create the atlas. The cited section of the Stodilka reference describes "the registration procedure" that "maps atlas space into patient-specific space," (column 7, lines 9-11). The registration procedure described by the Stodilka reference does not correct distortion of a magnetic resonance modality volume, it simply uses spatial transformations to map atlas space onto patient specific space. Thus, the Stodilka reference does not teach correcting distortion of a first magnetic resonance modality volume derived from a first subject that is used to create an atlas, as recited by independent claim 52.

The Stodilka reference further fails to disclose "*providing a second magnetic resonance modality volume pertaining to a second subject... correcting distortion of said second magnetic resonance modality volume; and updating said magnetic property data in node of said atlas....*," as recited by claim 52. As discussed above, Miller discloses an anatomical template formed from a single subject. The Stodilka reference discloses a cardiac atlas for simulating a SPECT or PET cardiac image "constructed by amalgamating a plurality of patient scans" (column 6, lines 60-67). The Stodilka reference teaches amalgamating scans from different patients to form a cardiac atlas, but amalgamating patient scans is not "*correcting distortion of said first magnetic resonance modality volume* [pertaining to a first subject]. . . *recording a magnetic property value in a node of said atlas corresponding to a voxel of said first magnetic modality volume. . . correcting distortion of said second magnetic resonance modality volume* [pertaining to a second patient]. . . *and updating said magnetic property data in node of said atlas*,"as recited by claim independent claims 52. Simply "amalgamating scans" does not teach or suggest the claimed method.

The Office Action asserts that the Miller reference teaches "determining statistical representation values including the mean and variance of intensities of each or a plurality of magnetic property values at each corresponding voxel of the plurality of subjects (page 11947, col.2 paragraph 5 – page 11946, col.1)." The cited section of the Miller reference describes determining "the transformation field **u**, which is the mean of the posterior distribution induced by the potential of Equation 2," (page 11945, column 2, paragraph5). The transformation field in the Miller reference refers to a spatial transformation that maps the spatial configuration of patient A onto the spatial configuration of the anatomical template. The "mean of the posterior distribution" has nothing to do with the mean and variance of magnetic property values of a

plurality of subjects. As discussed above, the Miller reference teaches an anatomical textbook including data from a single patient. The Miller reference does not teach "updating magnetic property data" in the atlas with data from a second subject.

The Stodilka reference and the Miller reference fail to teach or suggest correcting distortion of a first magnetic resonance modality volume pertaining to a first subject and storing the corresponding magnetic property value in a node and correcting distortion of a second magnetic resonance modality volume pertaining a second subject and updating said magnetic property data in a node of the atlas, as recited by claim 52. Thus, the Stodilka reference and the Miller reference, alone or in combination, fail to teach or suggest each and every element of independent claim 52, and its dependent claims 55 and 56, which are therefore allowable. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 52, 55 and 56.

Similar to claim 52, claim 57 recites a method of creating "*a prior probability MRI based atlas*" comprising "*providing a first magnetic resonance modality volume pertaining to a subject...correcting distortion of said first magnetic resonance modality volume... and recording magnetic property data... in a node of said atlas corresponding to a voxel of said first magnetic modality volume.*" As discussed above, the Stodilka reference and the Miller reference, alone or in combination, fail to teach or suggest "*a prior probability MRI based atlas*" comprising "*providing a first magnetic resonance modality volume pertaining to a subject...correcting distortion of said first magnetic resonance modality volume... and recording a magnetic property value... in a node of said atlas corresponding to a voxel of said first magnetic modality volume,*" as recited by claim 52. Thus the Stodilka reference and the Miller reference, alone or in combination, fail to teach or suggest the analogous elements of claim 57 which is therefore allowable. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of independent claim 57.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the Miller reference and the Stodilka reference, alone or in combination, fail to disclose, teach or suggest each and every element of claims 46-48, 50-52, 55-57, 69-74, 76-82, 84-89 and 92-101. Applicants respectfully request the Examiner to reconsider and to withdraw the current rejections and pass the claims into allowance.

In view of the foregoing amendments and remarks, it is respectfully submitted that this application is now in condition for allowance. Applicants courteously solicit allowance of the claims in the form of a Notice of Allowance. Should there be any outstanding issues of patentability following the entry of this response, a telephone interview is respectfully requested to resolve such issues.

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